INFECTIOUS ALLERGY

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At the present time in specialized literature very much attention is being given to the problems of allergic reactions. Several authors (Yegorov) consider that the capacity for allergic reactions is a characteristic of all living protoplasm and consequently all the living flesh on earth to some degree or other is subjected to the laws of allergy. Any deviation of the reactions of an organism from the average normal ones is considered by many authors as a manifestation of allergy which infinitely widens the bounds of the conception concerning allergy.

In this article we are not able to consider the problem of changed reactions of an organism in general and therefore we will limit ourselves to a brief review of the basic manifestations of only one of the types of these reactions, infectious allergy, which is observed during infection by the etiological agents of several infectious diseases and during intoxication by exotoxins.

As is known, during several infections (tuberculosis, tularemia, brucellosis, glanders, and others) a condition of increased sensitivity to the etiological agent is observed in the sick man or infected animals. In the majority of cases the indicator of this allergic condition is the skin reaction to various preparations prepared from the appropriate etiological agents (tularemia, tuberculosis, brucellosis) or the ophthalmic reaction (glanders).

While simultaneously studying the reaction of the skin and the cells of smooth muscles of the internal organs to bacterial antigens in animals infected with the etiological agents of brucellosis, tuberculosis, and glanders, we were convinced from abundant material that the reaction of skin cells to a bacterial endotoxin didn't reflect the true state of reactivity of the cells from the internal organs.

Experiments which make it possible to directly register the reaction of these cells to bacterial antigens may serve as direct evidence of the allergic condition of cells from internal organs. Numerous authors have studied the reaction of cells from isolated organs of sensitized animals, but these investigators had their attention centered on problems concerning the principles of

the manifestation of anaphylaxis. Our investigations, which were devoted to problems of the immunity of cells of smooth muscles in isolated organs of immune animals, inevitably had to lead us to the study of the nature of the reactions of cells of internal organs in infected animals.

For developing the condition of infectious allergy in cells from internal organs we infected guinea pigs with the etiological agents of infectious abortion, tuberculosis, glanders, and others. In 30-45 days after the infection the animals were slaughtered and their isolated organs (segments of the small intestines, the horn of the uterus) were placed in a Schultz-Dell apparatus for studying the reactivity of cells of smooth muscles in relation to the endotoxin of the corresponding etiological agents.

Jointly with N. V. Galanova and K. I. Matveyev, we were able to establish that the reaction of cells of the smooth muscles from isolated organs of infected animals to the bacterial endotoxin considerably exceeded the reaction of the same organs of normal animals to the same endotoxins.

The increased sensitivity of the cells of smooth muscles is strictly specific. The cells of smooth muscles from the isolated organs of guinea pigs infected with the etiological agent of brucellosis revealed an increased sensitivity only with the introduction of the endotoxin of the etiological agent of brucellosis of cattle with which the animals were infected, and reacted normally to the endotoxin of the etiological agent of brucellosis of sheep and swine. By its specificity this reaction of cells considerably surpassed serological reactions which as is known are not capable of differentiating the representatives of one and the same group of etiological agents.

The condition of increased sensitivity of cells of smooth muscles of infected animals may be observed over a very long period of time. However neither we nor other authors have followed this process to the end. There is basis to assume that the length of the condition of infectious allergy of cells depends on the length of the effect of the factor which caused it. Thus for example, we together with N. V. Galanova succeeded in establishing that the increased sensitivity of cells of smooth muscles of a type of infectious allergy caused by the introduction of small doses of diphteria toxin is replaced by the normal sensitivity of these cells four months from the last introduction of toxin. According to material from I. P. Zamuriy, increased sensitivity of cells of smooth muscles in guinea pigs infected with the brucellosis etiological agent was just as well expressed nine months after introduction as it was a month after infection.

It must be assumed that in the first and in the second case we have one and the same type of allergy but the effect of the factor causing the allergy in the first case rapidly terminated, but in the second case it was indefinitely prolonged.

The increased sensitivity of cells of smooth muscles due to a type of infectious allergy may be easily differentiated from the increased sensitivity of these same cells due to a type of anaphylaxis. The difference between these two reactions of one and the same cells consists of the following.

1. For the condition of anaphylaxis the presence of desensitization is characteristic after the introduction of the resolving dose of antigen. This situation was established by experiments both on an animal and on its isolated organs. The condition of infectious allergy of cells from internal organs is not replaced by the condition of desensitization after single or even numerous contact with the antigen. And what is more, increasing the dose of antigen for repeated contact with cells that are in a state of infectious allergy entails an even more expressed reaction of these cells and not their desensitization as is characteristic for the increased sensitivity due to a type of anaphylaxis of those same cells.

We also weren't able to desensitize guinea pigs infected with the brucellosis etiological agent by means of the repeated introduction of increasing doses of a killed culture of the same etiological agent.

2. An animal which is in a state of sensitization rapidly dies from anaphylactic shock upon the introduction of a resolving dose of antigen. If the dose of antigen wasn't sufficiently massive the anaphylactic shock is replaced by the complete recovery of the animal.

Upon the introduction of a resolving dose to an animal which is in a state of infectious allergy no shock of any kind sets in. The death of the animal may result after several hours and even days with the symptoms of a sharp aggravation of the infectious process.

3. For the condition of anaphylaxis it is characteristic that it can be passively transferred with the serum of a sensitized animal to a fresh animal. And what is more, any serum containing precipitins may cause sensitization when introduced to a fresh animal. The condition of infectious allergy cannot be transferred to a fresh animal by means of introducing serum to it from an animal which is in a state of infectious allergy. However it is necessary to have assurance that the serum taken from the animal which is in a state of infectious allergy doesn't contain live etiological agents of the infection.

4. The condition of sensitization due to a type of anaphylaxis in guinea pigs caused by a single introduction under the skin of normal serum may be detected in an animal for its entire life.

The condition of infectious allergy of those same animals caused by the introduction of diphteria exotoxin is replaced by normal sensitivity of the animals' cells four months after the last introduction of the toxin.

5. The restoration of the condition of sensitization after a period of time, specific for each species of animal, following the resolving introduction of antigen is characteristic for the condition of increased sensitivity due to a type of anaphylaxis (for guinea pigs 10-14 days, for rabbits 9-14 days, etc.).

Cells of smooth muscles of guinea pigs infected with the brucellosis etiological agent pass from a condition of infectious allergy to a state of immunity after repeated infection with a brucellosis etiological agent of the same strain, but then in the course of an undetermined period (observed for a period of 2-3 months) the condition of infectious allergy of these cells doesn't return anew.

6. The condition of sensitization of the animal to a protein antigen due to a type of anaphylaxis and the condition of infectious allergy may be created in one and the same animal simultaneously. Investigation of the reaction of cells of smooth muscles to both antigens shows that a single contact of an isolated organ with a protein antigen desensitizes it in relation to the latter, but not to the bacterial endotoxin. A single or multiple contact of the isolated organ with the bacterial endotoxin doesn't desensitize the cells of the smooth muscles neither in relation to the protein antigen nor in relation to the bacterial endotoxin.

7. One of the significant differences of the condition of infectious allergy of cells from the condition of increased sensitivity due to a type of anaphylaxis is that the condition of sensitization due to a type of anaphylaxis may be caused by the introduction of any antigen capable of leading to the formation of antibodies. Along with this, the mechanism of anaphylactic shock doesn't change. We succeeded in causing a condition of infectious allergy of cells from internal organs during the infection of just a specific group of etiological agents of infectious diseases (tuberculosis, brucellosis, glanders) and during the frequent daily administration of bacterial exotoxins.

In summarizing the data from our experiments we can assert that only an external similarity exists between a condition of sensitization stipulated by the introduction of the protein antigen and the condition of infectious allergy caused by the introduction of the etiological agents of some infectious diseases (tuberculosis, brucellosis, glanders, tularemia and intoxication by exotoxins). These two conditions of one and the same cells are principally different from each other in their nature and mechanism.

The role of infectious allergy of cells in the development of the infectious process and immunity still hasn't been sufficiently fully elucidated by anyone. At the present time coworkers of our laboratory are engaged in solving this very important problem. However it is already clear to us now that the therapeutic effect of serum therapy completely depends on the nature of the reaction of cells from internal organs to the bacterial toxin. If the cells of internal organs of an animal are in a state of infectious allergy to the bacterial toxin, the introduction of specific serum doesn't change the course of the intoxication process.